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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,883	12/15/2003	Diane Lipscombe	B0877.70026US00	6781

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
07/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,883	LIPSCOMBE ET AL.	
	Examiner	Art Unit	
	STEVEN H. STANDLEY	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 37-44* is/are pending in the application.

4a) Of the above claim(s) *3,4,39,40,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-2, 37-38, 41-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RCE

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/05/2006 has been entered.

2. Claims 1-4, and 37-44 are pending. Claims 3-4, 39, and 43-44 remain withdrawn. Claims 1-2, 37-38, 41 and 42 are under examination.

Rejections/Objections: Withdrawn

Claim Rejections - 35 USC § 103

3. Rejection of claims 1-2, 37-38, 41 and 42 under 35 USC § 102(a) is withdrawn due to applicant's amendment to exclude exon e37b. Written support for this amendment can be found on page 51 of the specification.

Rejections/Objections: New

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-2, 37-38, and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cell that recombinantly expresses Cav2.2 comprising SEQ ID NO: 45, does not reasonably provide enablement

for an isolated cell that recombinantly expresses Cav2.2 comprising exon e37a. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The invention is complex because it claims a cell expressing a Cav2.2 calcium channel comprising "exon e37a." This is complex because there are interspecies variations in intron-exon organization and splicing. The designation exon e37a refers to the location of the exon within the genomic structure. Thus, it may be present in some species, not in others, or in a different locus than 'e37.'

The prior art discloses that there are interspecies variations in the organization of introns and exons, as well as the existence of alternate splice forms of intron cassettes. For instance, Heidmann et al report that the intron-exon organization of 5HT-7 receptors is substantially different in humans versus rats, and that some splice variants that are present in humans are not in rats. Van der Leif et al. also indicate the CPT1B gene has

numerous splice variations in the human form that are not present in mouse (see abstract). These data suggest that outside of the species disclosed in the specification, 'e37a' may have no meaning at all with respect to defining any particular sequence or even function.

The two examples above indicate that the organization of genes across species are not predictable, and must be determined *ad hoc*. Therefor one of ordinary skill in the art would not be able to make and use the invention given the breadth of the claims, which include all species without limitation.

The specification provides limited working examples such as mouse rat and human sequences for what it terms 'exon e37a.' However, it does not determine, for instance, whether the same sequence and genomic structure exists for gallus gallus Cav2.2[e37a] (see Lu and Dunlap, 1999; see the rejection under 35 USC § 102). Lu and Dunlap provide a sequence that is more similar to e37a than e37b, which may indicate sequence variation or different alternatively splice sequences, which may indeed not be exon 37. The specification also encompasses variants, especially different splice variants (see page 15 of specification) of the channel other than the one claimed without limits on species and without describing the possible variants or differences in genomic structure across the multitude of species the claims encompass. Thus, the variants have no structural or functional limits.

Given the complexity of the invention, the contradictory and unpredictable prior art, and the lack of support by example or guidance, it would require undue

experimentation for one of skill in the art to make or use the invention commensurate with the scope of the claims.

5. Claims 1-2, 37-38, and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are to a genus of calcium channels expressing a genus of 'e37a.' Applicant provides written description for a few species, but the claims are not limited even to mammals. The claims are readable on any cav2.2 channel and whatever constitutes 'e37a,' which is defined only by the locus of the intron in the human gene. Thus, what 'e37a' might be in another species not disclosed is without any structure or function. In any other species it is not known what constitutes 'e37a.' Therefore applicant is not in possession of the full scope of the invention.

Applicant does provide a sequence for the claimed splice variation, but the claims do not recite it. Instead, the claims recite 'exon e37a,' which is an arbitrary name that does not identify the claimed invention except within humans, mice and rats. One of skill in the art would not readily recognize what constitutes the claimed invention, because of the unpredictability of the gene structure and the lack of structure or function in the recited claim.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of exons, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. *Revel*, 25 USPQ2d 1601 at 1606 (CMC 1993) and *Amgen Inc*. v. *Chugai Pharmaceutical Co. Ltd*., 18 USPQ2d 1016.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lu and Dunlap (1999) by.

Lu and Dunlap disclose a chick (*gallus gallus*) Cav2.2 channel comprising a splice variant with two changes and 3 conservative substitutions in the region encoded by 'exon 37a.' Moreover, the differences are entirely exclusive of the differences seen in 'exon e37b [see figure 2 the segment beginning at amino acid 1762 to amino acid 1795 of the chick sequence].' Lu and Dunlap perform experiments with the variant in HEK cells (see Figure4). Thus, absent evidence to the contrary, Lu and Dunlap teach an isolated cell expressing a Cav2.2 subunit comprising 'exon e37a (and not e37b),' which meets the limitations of claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 37, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lu and Dunlap (1999; from rejection above).

Claims 37 and 41 further limit claim 1 to either a neuron or an oocyte. Lu and Dunlap disclose the recombinant protein expressed in HEK cells. It would be obvious to one of ordinary skill in the art to express the channel in either neurons or Oocytes because these are just analogous test systems for exploring the function of the receptor and for testing potential compounds that may modulate the channel.

In both cases, one would have a reasonable expectation for success.

The motivation to use Oocytes is that they provide an isopotential environment for measuring electrophysiological changes and can easily be prepared *en masse*. The motivation to use neurons is to test the channel and modulatory compounds in the environment in which the channel normally operates.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Stucker can be reached on **(571) 272-0911**.

The fax number for the organization where this application or proceeding is assigned is **(571) 273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
7/10/08

/Bridget E Bunner/
Primary Examiner, Art Unit 1647